Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

Screening for peripheral artery disease and cardiovascular disease risk assessment with the ankle–brachial index in adults: U.S. Preventive Services Task Force recommendation statement.

Bibliographic Source(s)

U.S. Preventive Services Task Force. Screening for peripheral artery disease and cardiovascular disease risk assessment with the ankle-brachial index in adults: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2013 Sep 3;159(5):342-8. [17 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: U.S. Preventive Services Task Force. Screening for peripheral arterial disease: recommendation statement. Am Fam Physician. 2006 Feb 1;73(3):497-500.

Recommendations

Major Recommendations

The U.S. Preventive Services Task Force (USPSTF) grades its recommendations (A, B, C, D, or I) and identifies the levels of certainty regarding net benefit (High, Moderate, and Low). The definitions of these grades can be found at the end of the "Major Recommendations" field.

Summary of Recommendations and Evidence

The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for peripheral artery disease (PAD) and cardiovascular disease (CVD) risk assessment with the ankle–brachial index (ABI) in adults. (I statement)

Clinical Considerations

Patient Population Under Consideration

This recommendation applies to asymptomatic adults who do not have a known diagnosis of PAD, CVD, severe chronic kidney disease, or diabetes.

Assessment of Risk

In addition to older age, major risk factors for PAD include diabetes, smoking, hypertension, high cholesterol level, obesity, and physical inactivity,

with smoking and diabetes showing the strongest association. PAD is more common in men than in women and occurs at an earlier age in men, possibly in part because of the higher prevalence of smoking in men. Among healthy U.S. men aged 40 to 75 years without a history of CVD, the risk for PAD over 25 years in the absence of 4 conventional cardiovascular risk factors (smoking, hypertension, hypercholesterolemia, or type 2 diabetes) is rare (9 cases per 100,000 person-years). These 4 risk factors account for 75% of all cases of PAD, and at least 1 of them is present at the time of PAD diagnosis in 96% of men. Therefore, if screening is determined to be beneficial, it would probably be most beneficial to persons who are at increased risk for PAD and are not already receiving cardiovascular risk reduction interventions.

PAD is a manifestation of systemic atherosclerosis and is typically considered a predictor for other types of CVD (CAD or cerebrovascular disease) and CVD events, such as myocardial infarction (MI), cerebrovascular accident, and death. Patients with PAD are at increased risk for CVD events because of concomitant coronary and cerebrovascular disease.

Screening Tests

Resting ABI is the most commonly used test in screening for and detection of PAD in clinical settings, although variation in measurement protocols may lead to differences in the ABI values obtained. The ABI is calculated as the systolic blood pressure obtained at the ankle divided by the systolic blood pressure obtained at the brachial artery while the patient is lying down. A ratio of less than 1 (typically defined as <0.9) is considered abnormal and is commonly used to define PAD. Physical examination has low sensitivity for detecting mild PAD in asymptomatic persons.

Although femoral bruit, pulse abnormalities, or ischemic skin changes significantly increase the likelihood ratio for low ABI (≤0.9), these signs indicate moderate to severe obstruction or clinical signs of disease. Although often done, the clinical benefits and harms of screening for PAD with a physical examination have not been well-evaluated and are beyond the scope of this review.

In addition to its ability to detect PAD, an abnormal ABI may be a useful predictor of CVD morbidity and mortality. ABI measurement may increase the discrimination or calibration of existing CVD risk assessments apart from whether it accurately detects PAD. However, the number of patients with an abnormal ABI who also have other diseases or findings that would indicate treatment and whether there is value to these patients knowing they have an abnormal ABI is not clear.

Screening Intervals

No studies provided evidence about the intervals for screening for PAD with the ABI.

Treatment

Evidence shows that low-dose aspirin treatment in asymptomatic patients with a low ABI does not improve health outcomes and may increase bleeding. No trials provided evidence on other interventions to reduce CVD events or interventions that might delay the onset of lower extremity symptoms.

Suggestions for Practice Regarding the I Statement

In deciding whether to screen for PAD with the ABI in asymptomatic adults, clinicians should consider the following factors.

Potential Preventable Burden

The true prevalence of PAD in the general population is not known. Recent data from the National Health and Nutrition Examination Survey show that 5.9% of the U.S. population aged 40 years or older (7.1 million persons) has a low ABI (≤0.9). More than half of these persons do not have typical symptoms of PAD. The proportion of these patients who will go on to develop symptoms is not known; however, PAD is an indicator of CVD. Studies estimate that in persons with stable claudication but not critical ischemia, approximately 70% to 80% will remain stable over 5 years, whereas 10% to 20% will have worsening claudication and 1% to 2% will develop critical ischemia. Similar data are not available for asymptomatic patients with a low ABI.

Potential Harms

Although minimal harms are associated with the ABI test itself, downstream harms are possible. False-positive results, anxiety, labeling, and exposure to gadolinium or contrast dye if either magnetic resonance angiography (MRA) or computed tomography angiography (CTA) is used to confirm diagnosis may occur. Using the ABI in conjunction with Framingham Risk Score (FRS) results may reclassify a patient's risk. Given the uncertainty of the appropriateness of such reclassifications, patients could either be reclassified to a higher risk category and receive additional treatments with resulting adverse effects or be reclassified to a lower risk category and discontinue treatments that may be beneficial.

Cost

The cost of the ABI test is primarily in time and staff resources; performing the test in the office setting takes approximately 15 minutes. In addition, new equipment that performs pulse volume recordings or Doppler wave form tracings may need to be purchased. Providing this test to asymptomatic patients may divert time from other prevention activities that may be more beneficial to the patient.

Current Practice

In a survey of primary care practices across the United States, nearly 70% of providers reported never using the ABI in their practice settings, 6% to 8% reported using it once a year, and only 12% to 13% reported using it once a week or month.

Definitions:

What the U.S. Preventive Services Task Force (USPSTF) Grades Mean and Suggestions for Practice

Grade	Grade Definitions	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this service only if other considerations support offering or providing the service in an individual patient.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I Statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be measured.	Read "Clinical Considerations" section of USPSTF Recommendation Statement (see the "Major Recommendations" field). If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

USPSTF Levels of Certainty Regarding Net Benefit

Definition: The USPSTF defines *certainty* as "likelihood that the USPSTF assessment of the net benefit of a preventive service is correct." The net benefit is defined as benefit minus harm of the preventive service as implemented in a general, primary care population. The USPSTF assigns a certainty level based on the nature of the overall evidence available to assess the net benefit of a preventive service.

Level of Certainty	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by factors such as: • The number, size, or quality of individual studies • Inconsistency of findings across individual studies • Limited generalizability of findings to routine primary care practice; and • Lack of coherence in the chain of evidence As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be

Level of Certainty	Description
	large enough to alter the conclusion.
Low	The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of:
	• The limited number or size of studies • Important flaws in study design or methods • Inconsistency of findings across individual studies • Gaps in the chain of evidence • Findings not generalizable to routine primary care practice; and • A lack of information on important health outcomes More information may allow an estimation of effects on health outcomes.

Clinical Algorithm(s)

None available

Scope

Disease/Condition(s)

Peripheral artery disease (PAD)

Guideline Category

Prevention

Screening

Clinical Specialty

Cardiology

Family Practice

Geriatrics

Internal Medicine

Preventive Medicine

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Health Care Providers

Health Plans

Managed Care Organizations

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

- To review the evidence on the use of resting ankle-brachial index (ABI) as a screening test for peripheral artery disease (PAD) or as a risk predictor for cardiovascular disease (CVD)
- To update the 2005 U.S. Preventive Services Task Force (USPSTF) recommendation on screening for PAD

Target Population

Asymptomatic adults who do not have a known diagnosis of peripheral artery disease (PAD), cardiovascular disease (CVD), severe chronic kidney disease, or diabetes

Interventions and Practices Considered

Resting ankle–brachial index (ABI) as a screening test for peripheral artery disease (PAD) or as a risk predictor for cardiovascular disease (CVD)

Major Outcomes Considered

- Key Question 1: Is screening generally asymptomatic adults for peripheral arterial disease (PAD) using ankle-brachial index (ABI) effective in reducing cardiovascular disease (CVD) morbidity (e.g., myocardial infarction [MI], cardiovascular accident [CVA]), morbidity from PAD (e.g., amputation, impaired ambulation, impaired function), or mortality (e.g., CVD specific, overall)?
    a. Does the effectiveness of screening for PAD vary by subgroup (i.e., age [especially for age 65 years and older], sex, race, risk factors)?
- Key Question 2: In generally asymptomatic adults, what is the diagnostic accuracy (e.g., sensitivity, specificity, positive and negative predictive value) of ABI as a screening test for PAD?
    a. Does the diagnostic accuracy of ABI screening vary by subgroup (i.e., age [especially for age 65 years and older], sex, race, risk factors)?
- Key Question 3: What are the harms of screening (e.g., diagnostic inaccuracy [overdiagnosis], harms of additional testing)?
    a. Do the harms of screening vary by subgroup (i.e., age [especially for age 65 years and older], sex, race, risk factors)?
- Key Question 4: Does ABI in generally asymptomatic adults accurately predict CVD morbidity (e.g., MI, CVA) and mortality independent of traditional risk factors?
    a. What is the prevalence of a normal and abnormal ABI among low-, intermediate-, and high-risk adults?
    b. At what frequency does the use of ABI significantly change the risk of CVD morbidity or mortality based on traditional risk factors alone (e.g., from intermediate risk to low or high risk)?
    c. What is the accuracy of risk reclassification of CVD morbidity or mortality (in addition to traditional risk factors)?
- Key Question 5: Does treatment of asymptomatic or minimally symptomatic adults with PAD lead to improvement in patient outcomes beyond the benefits of treatment in symptomatic adults, or beyond the benefits of treatment of adults with known CVD risk factors (i.e., smoking, hypertension, hyperlipidemia)?
    a. Does the effectiveness of treatment vary by subgroup (i.e., age [especially for age 65 years and older], sex, race, risk factors)?
- Key Question 6: What are the harms of treatment of screen-detected PAD?
    a. Do the harms of treatment vary by subgroup (i.e., age [especially for age 65 years and older], sex, race, risk factors)?

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): An evidence synthesis was prepared by the Kaiser Permanente Research Affiliates Evidence-based Practice Center (EPC) for the U.S. Preventive Services Task Force (USPSTF) (see the "Availability of Companion Documents" field).

Data Sources and Searches

The EPC staff searched MEDLINE and the Cochrane Central Registry of Controlled Trials from 1996 through September 2012 to locate relevant English-language studies for all Key Questions. The staff supplemented searches with suggestions from experts and reference lists from 62 recent relevant existing systematic reviews. The staff also searched ClinicalTrials.gov on September 12, 2012 for relevant ongoing trials.

Study Selection

Two investigators independently reviewed 4,434 abstracts and 418 full-text articles (see Appendix D of the comparative effectiveness review) against the specified inclusion criteria (see Appendix E of the comparative effectiveness review). We resolved discrepancies by consultation with a third investigator. We list the studies we excluded at the full-text phase (i.e., based on exclusion criteria or for poor quality) in Appendix F of the comparative effectiveness review.

The review focuses on the clinical utility of resting ankle-brachial index (ABI) as the primary screening modality because it is the most commonly used and is able to detect asymptomatic persons. Therefore, this review excluded other methods of screening (e.g., questionnaires, exercise ABI, toe pressure measurement, pulse oximetry, duplex ultrasound, magnetic resonance angiography [MRA]). This review also focuses on generally asymptomatic adults, which may include populations with atypical symptoms or minor symptoms not recognized as peripheral arterial disease (PAD). The EPC staff excluded studies whose subjects primarily had known intermittent claudication. The staff also excluded studies conducted exclusively in persons with known cardiovascular disease (CVD), diabetes, or severe chronic kidney disease (stage 4 and 5). The staff excluded studies conducted in hospital or specialty settings (i.e., vascular clinics or laboratories), as these settings typically represented populations selected for known or highly suspected PAD. Because the focus is on largely asymptomatic persons, primary outcomes of interest are CVD events and risk factor reduction, rather than lower-extremity symptoms. If studies that met the inclusion criteria also reported PAD-specific outcomes (e.g., limb function, ambulation, amputation), however, the EPC staff considered these outcomes. Likewise, included treatments focused on pharmacologic or lifestyle interventions primarily aimed at CVD risk reduction (e.g., smoking cessation, cholesterol lowering, blood pressure control, and antiplatelet therapy). Therefore, the staff excluded interventions aimed primarily at management of lower-extremity symptoms or functioning (e.g., cilostazol, supervised exercise training or physical therapy, revascularization).

For Key Question (KQ) 1, the EPC staff considered any trial (randomized, controlled trial [RCT] or controlled clinical trial [CCT]) or systematic review that compared ABI screening to no screening reporting any outcome of interest (i.e., CVD or PAD-specific morbidity or mortality). For KQ 2, the staff considered prospectively conducted diagnostic accuracy studies or well-conducted systematic reviews of diagnostic accuracy. The staff excluded case-control studies in which cases were selected based on having known PAD. Distorted selection of subjects in recruitment or case-control designs has repeatedly been shown to overestimate sensitivity. A distorted selection of subjects directly affects the applicability of the study findings and threatens its validity (i.e., spectrum bias). Spectrum bias refers to the phenomenon that the diagnostic test performance may change between clinical settings due to changes in patient case-mix. For KQ 2, diagnostic accuracy studies had to compare ABI with a reference standard. Because the gold standard, digital subtraction angiography (DSA), is an invasive test that presents known risks, it is not ethical to administer this test in asymptomatic persons. Therefore, the staff considered any diagnostic test that could image the degree of atherosclerosis (e.g., MRA, computed tomography angiography [CTA]) or degree of impaired blood flow (e.g., duplex ultrasound) to be a reasonable diagnostic reference standard. The staff accepted all measures of diagnostic accuracy (e.g., sensitivity, specificity, positive or negative predictive values, positive or negative likelihood ratios). For KQ 4, the staff considered prospective longitudinal cohort studies or systematic reviews of risk prediction. Included risk prediction studies had to assess ABI in addition to existing Framingham Risk Score (FRS) factors, as defined in ATP III (i.e., age, sex, smoking status, systolic blood pressure, total cholesterol, and high-density lipoprotein [HDL] cholesterol). While studies could adjust for additional known risk factors, the staff excluded studies that did not consider all existing FRS factors as a minimum. For KQ 5, the staff included any trial (RCT or CCT) or systematic review with at least 12 weeks of follow-up that compared treatment of PAD with no treatment, with placebo treatment, or with delayed treatment. Again, the EPC staff considered any outcome of interest (i.e., CVD or PAD-specific morbidity or mortality). While the staff included reviews, trials, cohort studies, and case-control studies for KQs 3 and 6, case series or case reports were excluded.

Number of Source Documents

- Key Question 1: 0 articles
- Key Question 2: 2 articles
- Key Question 3: 1 article
- Key Question 4: 16 articles
- Key Question 5: 3 articles
- Key Question 6: 3 articles

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): An evidence synthesis was prepared by the Kaiser Permanente Research Affiliates Evidence-based Practice Center (EPC) for the U.S. Preventive Services Task Force (USPSTF) (see the "Availability of Companion Documents" field).

Data Extraction and Quality Assessment

For screening studies, the EPC staff extracted details about each study's location, recruitment, inclusion/exclusion criteria, participant characteristics, reference standard, test performance characteristics, and adverse events. For risk prediction studies, the staff extracted details about each study's location, recruitment, inclusion/exclusion criteria, participant characteristics, technique for measuring ankle-brachial index (ABI), adequacy and length of follow-up, method for ascertaining outcomes, inclusion of prognostic factors other than ABI, analytic approach, and outcomes. Outcomes included relative event outcomes (e.g., hazard ratio [HR], relative risk [RR], or overall risk [OR]) or measures of risk reclassification. Measures of discrimination or risk reclassification included differences in the area under the curve (AUC) or c-statistic, percent reclassified (i.e., from a reclassification table), and net reclassification improvement (NRI).

Risk reclassification refers to the change in risk when a new predictor is added to an existing risk prediction model (i.e., subjects may be placed into a different risk category than the one they were in when the original model was used). This movement between risk categories may be displayed as a reclassification table. This table shows the number (and percent) of subjects in each risk category using the original model versus the number (and percent) of subjects in each risk category using the model with the new predictor. While studies may report the percent of subjects who change risk categories, this does not ensure subjects were correctly recategorized. Subjects who will have an outcome event should move to a higher risk category, while subjects who will not have an event should move to a lower risk category. For subjects who will have an event, movement to a higher risk category is improved classification, while movement to a lower risk category is worse (incorrect) classification; likewise, for subjects who will not have an event, movement to a lower risk category is improved classification, while movement to a higher risk category is worse classification. The NRI quantifies this as (proportion of subjects who will have an event moving higher minus proportion of subjects who will have an event moving lower) + (proportion of subjects who will not have an event moving lower minus proportion of subjects who will not have an event moving higher). Another way to think of the NRI is the sum of the improvement in sensitivity and the improvement in specificity.

In a risk reclassification table, those cells representing no change in risk category between prediction models lie on a diagonal; the other cells represent a change in risk between the original model and the new model. If the original and new prediction models were the same, the numbers in the cells representing change would be symmetric about the cells representing no change. The number of subjects who will have an event moving to

a higher risk category would equal the number moving to a lower risk category and the number of subjects who will not have an event moving to a lower risk category would equal the number moving to a higher risk category. If an NRI were calculated for the entire table, it would be zero. However, an NRI might be calculated only for certain risk categories, as defined by the original model. Only those cells lying in certain rows of the risk reclassification table would be used, and some of the symmetric cells from the reclassification table would be excluded. An NRI could be calculated; if it were positive, it would imply improvement, even though the models were identical. Therefore, an NRI for any subset of risk categories will be artificially inflated by this expected NRI simply because some of the symmetrically distributed cells are excluded. A corrected NRI may be calculated by subtracting the expected NRI from the apparent NRI. For risk prediction studies reporting NRI for subgroups (i.e., intermediate-risk groups), the EPC staff calculated a corrected NRI for the intermediate risk category where data were available to do so.

The AUC—specifically, the area under the receiver operating characteristic curve—represents a model's ability to discriminate between subjects who will and will not have an event. The AUC is the probability that a model will assign a higher risk for an event to a randomly selected subject who will have an event than to a randomly selected subject who will not have an event. The range of the AUC is 0.5 (no discriminatory ability) to 1 (perfect discrimination). For prognostic models, the AUC is typically 0.6 to 0.85. When a new predictor is added to a model, the improvement in the model's ability to discriminate may be measured by the difference between the AUC for the model with the new predictor and the AUC for the original model. An increase in the AUC of 0.025 is considered clinically relevant.

For treatment trials, the EPC staff extracted details about each study's location, recruitment, inclusion/exclusion criteria, patient characteristics, experimental and comparison intervention(s), internal validity, retention, method for ascertaining outcomes, analytic approach, outcomes, and adverse effects. A second reviewer verified all extracted data. The staff contacted study authors by email for clarification, when necessary.

At least two reviewers independently critically appraised articles meeting inclusion criteria using the USPSTF's design-specific quality criteria, supplemented with the National Institute for Health and Care Excellence (NICE) methodology checklists, Quality Assessment of Diagnostic Accuracy Studies (for studies of diagnostic accuracy [KQ 2]), and the Newcastle-Ottawa Scale and Hayden criteria (for prediction studies [KQ 4]). Articles were rated as good, fair, or poor quality. In general, a good-quality study met all criteria well. A fair-quality study did not meet (or it was unclear whether it met) at least one criterion but also had no known important limitation that could invalidate its results. A poor-quality study had a single fatal flaw or multiple important limitations. The most common flaws leading to poor-quality ratings among studies about diagnostic accuracy were having an inappropriate reference standard, a biased spectrum of subjects, or verification bias. The most common flaw leading to poor-quality ratings among studies about prognosis was lack of relevant outcomes. However, the majority of prognostic studies were excluded because they did not include all the Adult Treatment Panel (ATP) III FRS factors in multivariable models and therefore did not meet the inclusion criteria. For treatment trials, the staff excluded the majority of studies because they were conducted in persons with intermittent claudication. The staff excluded poor-quality studies from this review.

Synthesis and Analysis

The EPC staff did not conduct any quantitative analyses for any of the KQs due to the low volume, heterogeneity, and nature of our included studies. They found no studies for KQ 1. For KQs 2 and 3, the staff included only one study and therefore describe the results of this single study along with the quality and applicability assessment. For KQ 4, the staff included 14 studies representing eight different cohorts and one large individual patient-level data meta-analysis. The meta-analysis included all but two of the cohorts represented in the 14 other studies. Given the available information, the staff was unable to attempt further quantitative syntheses. Instead, they qualitatively synthesized data from this pooled analysis, comparing and contrasting its results with findings from individual studies by outcomes, focusing primarily on measures of risk reclassification and secondarily on measures of association (HR and RR) adjusted for FRS factors (i.e., age, sex, smoking status, systolic blood pressure, total cholesterol, HDL cholesterol). They use summary tables to display differences between important study characteristics and outcomes across included studies. For KQs 5 and 6, the staff included only two treatment studies that were quite different from one another. Therefore, the staff summarizes the results of these studies in the context of their quality and applicability.

For each KQ, the EPC staff summarizes the overall body of evidence, commenting on several domains, including quality of findings (including risk of bias), applicability of findings, consistency of findings (including possible clinical heterogeneity explaining inconsistencies), magnitude of findings, and precision around the magnitude of findings.

Methods Used to Formulate the Recommendations

Balance Sheets

Expert Consensus

Description of Methods Used to Formulate the Recommendations

The U.S. Preventive Services Task Force (USPSTF) systematically reviews the evidence concerning both the benefits and harms of widespread implementation of a preventive service. It then assesses the certainty of the evidence and the magnitude of the benefits and harms. On the basis of this assessment, the USPSTF assigns a letter grade to each preventive service signifying its recommendation about provision of the service (see table below). An important, but often challenging, step is determining the balance between benefits and harms to estimate "net benefit" (that is, benefits minus harms).

Table 1. U.S. Preventive Services Task Force Recommendation Grid*

Certainty of Net Benefit	Magnitude of Net Benefit			
	Substantial	Moderate	Small	Zero/Negative
High	A	B	C	D
Moderate	B	B	C	D
Low	Insufficient			

**A, B, C, D*, and *I (Insufficient)* represent the letter grades of recommendation or statement of insufficient evidence assigned by the U.S. Preventive Services Task Force after assessing certainty and magnitude of net benefit of the service (see the "Rating Scheme for the Strength of the Recommendations" field).

The overarching question that the Task Force seeks to answer for every preventive service is whether evidence suggests that provision of the service would improve health outcomes if implemented in a general primary care population. For screening topics, this standard could be met by a large randomized, controlled trial (RCT) in a representative asymptomatic population with follow-up of all members of both the group "invited for screening" and the group "not invited for screening."

Direct RCT evidence about screening is often unavailable, so the Task Force considers indirect evidence. To guide its selection of indirect evidence, the Task Force constructs a "chain of evidence" within an analytic framework. For each key question, the body of pertinent literature is critically appraised, focusing on the following 6 questions:

1. Do the studies have the appropriate research design to answer the key question(s)?
2. To what extent are the existing studies of high quality? (i.e., what is the internal validity?)
3. To what extent are the results of the studies generalizable to the general U.S. primary care population and situation? (i.e., what is the external validity?)
4. How many studies have been conducted that address the key question(s)? How large are the studies? (i.e., what is the precision of the evidence?)
5. How consistent are the results of the studies?
6. Are there additional factors that assist the USPSTF in drawing conclusions (e.g., presence or absence of dose–response effects, fit within a biologic model)?

The next step in the Task Force process is to use the evidence from the key questions to assess whether there would be net benefit if the service were implemented. In 2001, the USPSTF published an article that documented its systematic processes of evidence evaluation and recommendation development. At that time, the Task Force's overall assessment of evidence was described as good, fair, or poor. The Task Force realized that this rating seemed to apply only to how well studies were conducted and did not fully capture all of the issues that go into an overall assessment of the evidence about net benefit. To avoid confusion, the Task Force has changed its terminology. Whereas individual study quality will continue to be characterized as good, fair, or poor, the term certainty will now be used to describe the Task Force's assessment of the overall body of evidence about net benefit of a preventive service and the likelihood that the assessment is correct. Certainty will be determined by considering all 6 questions listed above; the judgment about certainty will be described as high, moderate, or low.

In making its assessment of certainty about net benefit, the evaluation of the evidence from each key question plays a primary role. It is important to note that the Task Force makes recommendations for real-world medical practice in the United States and must determine to what extent the evidence for each key question—even evidence from screening RCTs or treatment RCTs—can be applied to the general primary care population. Frequently, studies are conducted in highly selected populations under special conditions. The Task Force must consider differences between the general primary care population and the populations studied in RCTs and make judgments about the likelihood of observing the same effect in actual practice.

It is also important to note that one of the key questions in the analytic framework refers to the potential harms of the preventive service. The Task Force considers the evidence about the benefits and harms of preventive services separately and equally. Data about harms are often obtained from observational studies because harms observed in RCTs may not be representative of those found in usual practice and because some harms are not completely measured and reported in RCTs.

Putting the body of evidence for all key questions together as a chain, the Task Force assesses the certainty of net benefit of a preventive service by asking the 6 major questions listed above. The Task Force would rate a body of convincing evidence about the benefits of a service that, for example, derives from several RCTs of screening in which the estimate of benefits can be generalized to the general primary care population as "high" certainty (see the "Rating Scheme for the Strength of the Recommendations" field). The Task Force would rate a body of evidence that was not clearly applicable to general practice or has other defects in quality, research design, or consistency of studies as "moderate" certainty. Certainty is "low" when, for example, there are gaps in the evidence linking parts of the analytic framework, when evidence to determine the harms of treatment is unavailable, or when evidence about the benefits of treatment is insufficient. Table 4 in the methodology document listed below (see the "Availability of Companion Documents" field) summarizes the current terminology used by the Task Force to describe the critical assessment of evidence at all 3 levels: individual studies, key questions, and overall certainty of net benefit of the preventive service.

Sawaya GF et al. Update on the methods of the U.S. Preventive Services Task Force: estimating certainty and magnitude of net benefit. Ann Intern Med. 2007;147:871-875. [5 references].

I Statements

For I statements, the USPSTF has a new plan to commission its Evidence-based Practice Centers to collect information in 4 domains pertinent to clinical decisions about prevention and to report this information routinely. This plan is described in the paper: Petitti DB et al. Update on the methods of the U.S. Preventive Services Task Force: insufficient evidence. Ann Intern Med. 2009;150:199-205. www.annals.org

The first domain is potential preventable burden of suffering from the condition. When evidence is insufficient, provision of an intervention designed to prevent a serious condition (such as dementia) might be viewed more favorably than provision of a service designed to prevent a condition that does not cause as much suffering (such as rash). The USPSTF recognized that "burden of suffering" is subjective and involves judgment. In clinical settings, it should be informed by patient values and concerns.

The second domain is potential harm of the intervention. When evidence is insufficient, an intervention with a large potential for harm (such as major surgery) might be viewed less favorably than an intervention with a small potential for harm (such as advice to watch less television). The USPSTF again acknowledges the subjective nature and the difficulty of assessing potential harms: for example, how bad is a "mild" stroke?

The third domain is cost—not just monetary cost, but opportunity cost, in particular the amount of time a provider spends to provide the service, the amount of time the patient spends to partake of it, and the benefits that might derive from alternative uses of the time or money for patients, clinicians, or systems. Consideration of clinician time is especially important for preventive services with only insufficient evidence because providing them could "crowd out" provision of preventive services with proven value, services for conditions that require immediate action, or services more desired by the patient. For example, a decision to routinely inspect the skin could take up the time available to discuss smoking cessation, or to address an acute problem or a minor injury that the patient considers important.

The fourth domain is current practice. This domain was chosen because it is important to clinicians for at least 2 reasons. Clinicians justifiably fear that not doing something that is done on a widespread basis in the community may lead to litigation. More important, addressing patient expectations is a crucial part of the clinician–patient relationship in terms of building trust and developing a collaborative therapeutic relationship. The consequences of not providing a service that is neither widely available nor widely used are less serious than not providing a service accepted by the medical profession and thus expected by patients. Furthermore, ingrained care practices are difficult to change, and efforts should preferentially be directed to changing those practices for which the evidence to support change is compelling.

Although the reviewers did not explicitly recognize it when these domains were chosen, the domains all involve consideration of the potential consequences—for patients, clinicians, and systems—of providing or not providing a service. Others writing about medical decision making in the face of uncertainty have suggested that the consequences of action or inaction should play a prominent role in decisions.

Rating Scheme for the Strength of the Recommendations

What the U.S. Preventive Services Task Force (USPSTF) Grades Mean and Suggestions for Practice

Grade	Grade Definitions	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this service only if other considerations support offering or providing the service in an individual patient.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I Statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be measured.	Read "Clinical Considerations" section of USPSTF Recommendation Statement (see the "Major Recommendations" field). If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

USPSTF Levels of Certainty Regarding Net Benefit

Definition: The USPSTF defines *certainty* as "likelihood that the USPSTF assessment of the net benefit of a preventive service is correct." The net benefit is defined as benefit minus harm of the preventive service as implemented in a general, primary care population. The USPSTF assigns a certainty level based on the nature of the overall evidence available to assess the net benefit of a preventive service.

Level of Certainty	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by factors such as: • The number, size, or quality of individual studies • Inconsistency of findings across individual studies • Limited generalizability of findings to routine primary care practice; and • Lack of coherence in the chain of evidence As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.
Low	The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of: • The limited number or size of studies • Important flaws in study design or methods • Inconsistency of findings across individual studies • Gaps in the chain of evidence • Findings not generalizable to routine primary care practice; and • A lack of information on important health outcomes More information may allow an estimation of effects on health outcomes.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Comparison with Guidelines from Other Groups

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Peer Review. Before the U.S. Preventive Services Task Force (USPSTF) makes its final determinations about recommendations on a given preventive service, the Evidence-based Practice Center and the Agency for Healthcare Research and Quality send a draft evidence review to 4 to 6 external experts and to Federal agencies and professional and disease-based health organizations with interests in the topic. The experts are asked to examine the review critically for accuracy and completeness and to respond to a series of specific questions about the document. After assembling these external review comments and documenting the proposed response to key comments, the topic team presents this information to the USPSTF in memo form. In this way, the USPSTF can consider these external comments before it votes on its recommendations about the service. Draft recommendation statements are then circulated for comment among reviewers representing professional societies, voluntary organizations, and Federal agencies, as well as posted on the Task Force Web site for public comment. These comments are discussed before the final recommendations are confirmed.

Response to Public Comment. A draft version of this recommendation statement was posted for public comment on the USPSTF Web site from 19 March to 15 April 2013. The USPSTF received few comments, several of which agreed with the recommendation. Some comments provided additional studies and different interpretations of the evidence reviewed by the USPSTF. The USPSTF reviewed all of these studies and determined that they did not provide the necessary evidence to change its conclusions because the recommendation focuses on asymptomatic adults who do not have a known diagnosis of peripheral artery disease (PAD), cardiovascular disease (CVD), severe chronic kidney disease, or diabetes and are treated in a primary care setting.

Comparison with Guidelines from Other Groups. Recommendations for screening from the following groups were discussed: American College of Cardiology Foundation and the American Heart Association (AHA).

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is not specifically stated for each recommendation.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Benefits of Detection and Early Treatment

The U.S. Preventive Services Task Force (USPSTF) found no evidence that screening for and treatment of peripheral arterial disease (PAD) in asymptomatic patients leads to clinically important benefits. It also reviewed the potential benefits of adding the ankle-brachial index (ABI) to the Framingham Risk Score (FRS) and found evidence that this results in some patient risk reclassification; however, how often the reclassification is appropriate or whether it results in improved clinical outcomes is not known.

Determining the overall benefit of ABI testing requires not only evidence on appropriate risk reclassification but also evidence that this

reclassification leads to treatments shown to improve clinical outcomes. One randomized trial found that aspirin did not reduce CVD events in patients with a low ABI. No studies assessed the effect of lipid-lowering therapy or other cardiovascular risk reduction interventions in patients with asymptomatic PAD and no known diagnosis of CVD or diabetes. The USPSTF found inadequate evidence that early treatment of screen-detected PAD leads to improvement in clinical outcomes.

Potential Harms

Harms of Detection and Early Treatment

The U.S. Preventive Services Task Force (USPSTF) found no studies addressing the magnitude of harms of screening for peripheral arterial disease (PAD) with the ankle-brachial index (ABI); however, the direct harms to the patient of screening itself, beyond the time needed for the test, are probably minimal. Other harms resulting from testing may include false-positive results, exposure to gadolinium or contrast dye if magnetic resonance angiography (MRA) or computed tomography angiography (CTA) is used to confirm diagnosis, anxiety, labeling, and opportunity costs.

The USPSTF found inadequate evidence on the harms of early treatment of screen-detected PAD. One study showed that low-dose aspirin treatment in asymptomatic patients with a low ABI may increase bleeding. Additional harms associated with treatment include use of unnecessary medications (or higher doses) and their resulting adverse effects and discontinuation of medications known to be effective in patients with established coronary artery disease (CAD) if the patient is reclassified to a lower risk category on the basis of a normal ABI.

Qualifying Statements

Qualifying Statements

- Recommendations made by the U.S. Preventive Services Task Force (USPSTF) are independent of the U.S. government. They should not be construed as an official position of the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.
- The USPSTF makes recommendations about the effectiveness of specific preventive care services for patients without related signs or symptoms.
- It bases its recommendations on the evidence of both the benefits and harms of the service and an assessment of the balance. The USPSTF does not consider the costs of providing a service in this assessment.
- The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision making to the specific patient or situation. Similarly, the USPSTF notes that policy and coverage decisions involve considerations in addition to the evidence of clinical benefits and harms.

Implementation of the Guideline

Description of Implementation Strategy

The experiences of the first and second U.S. Preventive Services Task Force (USPSTF), as well as that of other evidence-based guideline efforts, have highlighted the importance of identifying effective ways to implement clinical recommendations. Practice guidelines are relatively weak tools for changing clinical practice when used in isolation. To effect change, guidelines must be coupled with strategies to improve their acceptance and feasibility. Such strategies include enlisting the support of local opinion leaders, using reminder systems for clinicians and patients, adopting standing orders, and audit and feedback of information to clinicians about their compliance with recommended practice.

In the case of preventive services guidelines, implementation needs to go beyond traditional dissemination and promotion efforts to recognize the added patient and clinician barriers that affect preventive care. These include clinicians' ambivalence about whether preventive medicine is part of their job, the psychological and practical challenges that patients face in changing behaviors, lack of access to health care or of insurance coverage for preventive services for some patients, competing pressures within the context of shorter office visits, and the lack of organized systems in most practices to ensure the delivery of recommended preventive care.

Dissemination strategies have changed dramatically in this age of electronic information. While recognizing the continuing value of journals and other print formats for dissemination, the USPSTF Task Force will make all its products available through its Web site . The

combination of electronic access and extensive material in the public domain should make it easier for a broad audience of users to access USPSTF materials and adapt them for their local needs. Online access to USPSTF products also opens up new possibilities for the appearance of the annual, pocket-size *Guide to Clinical Preventive Services*.

To be successful, approaches for implementing prevention have to be tailored to the local level and deal with the specific barriers at a given site, typically requiring the redesign of systems of care. Such a systems approach to prevention has had notable success in established staff-model health maintenance organizations, by addressing organization of care, emphasizing a philosophy of prevention, and altering the training and incentives for clinicians. Staff-model plans also benefit from integrated information systems that can track the use of needed services and generate automatic reminders aimed at patients and clinicians, some of the most consistently successful interventions. Information systems remain a major challenge for individual clinicians' offices, however, as well as for looser affiliations of practices in network-model managed care and independent practice associations, where data on patient visits, referrals, and test results are not always centralized.

Implementation Tools

Foreign Language Translations

Mobile Device Resources

Patient Resources

Pocket Guide/Reference Cards

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

U.S. Preventive Services Task Force. Screening for peripheral artery disease and cardiovascular disease risk assessment with the ankle-brachial index in adults: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2013 Sep 3;159(5):342-8. [17 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2006 Feb (revised 2013 Sep 3)

Guideline Developer(s)

U.S. Preventive Services Task Force - Independent Expert Panel

Guideline Developer Comment

The U.S. Preventive Services Task Force (USPSTF) is a federally-appointed panel of independent experts. Conclusions of the USPSTF do not necessarily reflect policy of the U.S. Department of Health and Human Services (DHHS) or its agencies.

Source(s) of Funding

The U.S. Preventive Services Task Force (USPSTF) is an independent, voluntary body. The U.S. Congress mandates that the Agency for Healthcare Research and Quality support the operations of the USPSTF.

Guideline Committee

U.S. Preventive Services Task Force (USPSTF)

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**Members of the USPSTF at the time this recommendation was finalized. For a list of current Task Force members, go to http://www.uspreventiveservicestaskforce.org/Page/Name/our-members*.

Financial Disclosures/Conflicts of Interest

The U.S. Preventive Services Task Force (USPSTF) has an explicit policy concerning conflict of interest. All members disclose at each meeting if they have a significant financial, professional/business, or intellectual conflict for each topic being discussed. USPSTF members with conflicts may be recused from discussing or voting on recommendations about the topic in question.

Potential Conflicts of Interest: Dr. Moyer: Support for travel to meetings for the study and other purposes: Agency for Healthcare Research and Quality. Disclosure forms from USPSTF members can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M13-1670.

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: U.S. Preventive Services Task Force. Screening for peripheral arterial disease: recommendation statement. Am Fam Physician. 2006 Feb 1;73(3):497-500.

Guideline Availability

Electronic copies: Available from the Annals of Internal Medicine Web site .

Availability of Companion Documents

The following are available:

Evidence Reviews:

- Lin JS, Olson CM, Johnson ES, Senger CA, Soh CB, Whitlock EP. The ankle–brachial index for peripheral artery disease screening and cardiovascular disease prediction among asymptomatic adults: a systematic evidence review for the U.S. Preventive Services Task Force. Ann Intern Med. 2013;159:333-341.
- Lin JS, Olson CM, Johnson ES, Senger CA, Soh CB, Whitlock EP. The ankle brachial index for peripheral artery disease screening and cardiovascular disease prediction in asymptomatic adults: a systematic evidence review for the U.S. Preventive Services Task Force. Evidence synthesis No. 100. AHRQ Publication No. 12-05162-EF-1. Rockville (MD): Agency for Healthcare Research and Quality; 2013 Sep. 112 p.

Electronic copies: Available from the U.S. Preventive Services Task Force (USPSTF) Web site .

Background Articles:

- Barton MB et al. How to read the new recommendation statement: methods update from the U.S. Preventive Services Task Force. Ann Intern Med 2007;147:123-127.
- Guirguis-Blake J et al. Current processes of the U.S. Preventive Services Task Force: refining evidence-based recommendation development. Ann Intern Med 2007;147:117-122.
- Sawaya GF et al. Update on the methods of the U.S. Preventive Services Task Force: estimating certainty and magnitude of net benefit. Ann Intern Med 2007;147:871-875.
- Petitti DB et al. Update on the methods of the U.S. Preventive Services Task Force: insufficient evidence. Ann Intern Med. 2009;150:199-205.

Electronic copies: Available from the USPSTF Web site .

The following are also available:

- Screening for peripheral artery disease and cardiovascular disease risk assessment with the ankle–brachial index in adults. Clinical summary of U.S. Preventive Services Task Force Recommendations. Rockville (MD): Agency for Healthcare Research and Quality; 2013 Sep. Electronic copies: Available from the USPSTF Web site .
- The guide to clinical preventive services, 2012. Recommendations of the U.S. Preventive Services Task Force. Rockville (MD): Agency for Healthcare Research and Quality (AHRQ); 2012. 128 p. Electronic copies available from the AHRQ Web site . See the related QualityTool summary on the Health Care Innovations Exchange Web site .

The Electronic Preventive Services Selector (ePSS) is an application designed to provide primary care clinicians and health care teams timely decision support regarding appropriate screening, counseling, and preventive services for their patients. It is based on the current, evidence-based recommendations of the USPSTF and can be searched by specific patient characteristics, such as age, sex, and selected behavioral risk factors.

Patient Resources

The following are available:

- Understanding task force recommendations: screening for peripheral artery disease and cardiovascular disease risk assessment with the ankle-brachial index in adults. Rockville (MD): Agency for Healthcare Research and Quality; 2013 Sep. 3 p. Electronic copies: Available from the U.S. Preventive Services Task Force (USPSTF) Web site .
- Screening for peripheral artery disease and cardiovascular disease risk assessment with the ankle-brachial index in adults. U.S. Preventive Services Task Force recommendation statement. Summary for patients. Ann Intern Med. 2013 Sep 3;159(5):I-28. Electronic copies: Available from the Annals of Internal Medicine Web site .
- Women: stay healthy at any age. Rockville (MD): Agency for Healthcare Research and Quality (AHRQ). AHRQ Pub. No. 10-IP002-A. 2010 Aug. 2 p. Electronic copies: Available in Portable Document Format (PDF) in English and Spanish from the AHRQ Web site. See the related QualityTool summary on the Health Care Innovations Exchange Web site .
- Men: stay healthy at any age. Rockville (MD): Agency for Healthcare Research and Quality. AHRQ Pub. No. 10-IP004-A. 2010 Aug. 2 p. Electronic copies: Available in PDF in English and Spanish from the AHRQ Web site. See the related QualityTool summary on the Health Care Innovations Exchange Web site .

Print copies: Available in English and Spanish from the AHRQ Publications Clearinghouse. For more information, go to http://www.ahrq.gov/research/publications/index.html or call 1-800-358-9295 (U.S. only).

Myhealthfinder is a new tool that provides personalized recommendations for clinical preventive services specific to the user's age, gender, and pregnancy status. It features evidence-based recommendations from the USPSTF and is available at www.healthfinder.gov .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

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